This guidance was written prior to the February 27, 1997 implementation of FDA's Good Guidance Practices, GGP's. It does not create or confer rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. This guidance will be updated in the next revision to include the standard elements of GGP's.

Regulatory Requirements For Devices For the Handicapped

U.S. Department of Health and Human Services
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Center for Devices and Radiological Health

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Regulatory Requirements For Devices For the Handicapped

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PREFACE

New medical devices can greatly benefit the disabled and handicapped, opening new vistas of health, ability to function, and quality of life. Such products are regulated by the Center for Devices and Radiological Health (CDRH), Food and Drug Administration (FDA). This booklet briefly explains FDA requirements for medical devices for the handicapped or disabled. It is part of an overall program by the Department of Health and Human Services (HHS) to encourage design and manufacture of such medical products, which often are in desperate need. HHS recognizes that such devices frequently produce little or no profit, and often are developed by small businesses with scant knowledge of government procedures.

This publication will be useful as a guide to manufacturers of devices for the handicapped in meeting regulatory requirements in such areas as establishment registration, device listing, labeling, classification, premarket notification [the 510(k) process], and premarket approval (PMA). In addition, the following pages explain how manufacturers can get help in meeting FDA requirements.

In this regard, the Medical Device Amendments of 1976 mandated "...an identifiable office to provide technical and other nonfinancial assistance to small manufacturers of medical devices to assist them in complying with the requirements of the Federal Food, Drug, and Cosmetic Act." The Division of Small Manufacturers Assistance (DSMA), in the Office of Training and Assistance, was established to meet these requirements. DSMA sponsors workshops and conferences to provide small device firms with a working knowledge of device requirements and compliance policies.

For further information, contact the appropriate CDRH division or call DSMA toll free at (800) 638-2041. Comments on this booklet and other Center activities are always welcome.

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ABSTRACT

Stigi, J., and R. J. Rivera. Regulatory Requirements for Devices for the Handicapped. HHS Publication FDA 87-4221 (1987) (28 pp.). This booklet explains the basic regulatory requirements that manufacturers must consider when they manufacture, market or distribute a medical device for the disabled or handicapped. The information is useful compliance guidance for such areas as establishment registration, device listing, premarket notification, premarket approval, investigational device exemptions, good manufacturing practices, and custom devices.

REGULATORY REQUIREMENTS FOR DEVICES FOR THE HANDICAPPED

WHO IS A HANDICAPPED PERSON?

Section 504 of the Rehabilitation Act Amendments of 1974 identifies a handicapped person as anyone with a physical or mental impairment that substantially limits one or more such major life activities as walking, seeing, hearing, speaking, working or learning. A history of such disability, or the belief on the part of others, whether accurate or not, that a person has such a disability, is also recognized as a handicap.

WHAT IS A DEVICE?

The Federal Food, Drug, and Cosmetic (FD&C) Act defines a "device" as "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is

- "recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,
- "intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
- "intended to affect the structure or any function of the body of man or other animals, and
- "which does not achieve any of its principal intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its principal intended purposes."

Devices that aid the handicapped will "affect the structure or any function of the body" and clearly meet the definition of a medical device. Examples of such devices are hearing aids, eyeglass lenses and frames, prostheses, powered exercise equipment, manual walkers, and wheelchairs.

Some devices may be regulated by more than one law. For example, radiation-emitting medical devices, such as microwave, shortwave or ultrasound diathermy devices for use in applying therapeutic deep heat for selected medical conditions, must comply with the FD&C Act and the Radiation Control for Health and Safety Act. If you are not sure if the device is regulated under more than one Act, you can contact the Center for Devices and Radiological Health (CDRH), Division of Product Surveillance (301-427-8156) or Division of Small Manufacturers Assistance (DSMA) (800-638-2041).

DEVICE CATEGORIES

CLASSIFICATION OF MEDICAL DEVICES

The FD&C Act requires FDA to place all devices intended for human use into one of the three classes. These classes are assigned according to the amount of control needed to assure the safety and effectiveness of each device.

Class I: General Controls

This class is for devices for which minimum controls are sufficient to assure their safety and effectiveness. These minimum requirements also apply to Class II and III devices. Included in these controls are:

- Registration of domestic device manufacturers and importers of foreign-made devices
- Listing of marketed devices by domestic and foreign manufacturers
- Premarket notification
- Restriction of the sale, distribution, or use of certain devices
- Good manufacturing practices (GMPs) to be adhered to when manufacturing medical devices
- Regulations that allow FDA to ban devices from the market place if they prove to be a health hazard

Certain Class I devices may be exempted from submission of a premarket notification [510(k)] and from portions of the GMPs. If a device has been exempted from either or both of the above, the exemption is noted in the final classification regulation for that particular device.

Many devices for the handicapped have been placed into Class I, mainly because they are simple devices that present little harm to the user. Examples of these are canes, crutches, and mechanical wheelchairs.

Class II: Performance Standards

This class is for devices for which general controls alone are insufficient to assure safety and effectiveness and for which there is enough information to write a performance standard. These devices must then comply not only with the general controls, but also with the applicable performance standard. Until a performance standard is finalized by regulation, only general controls apply.

The bulk of medical devices have been placed in Class II. Devices for the handicapped such as mechanical automobile hand-and-foot controls, powered environmental control system, and eyeglass lenses and frames are all examples of Class II products.

Class III: Premarket Approval

This class is for devices for which insufficient information exists to assure that general controls and performance standards will provide reasonable assurance of safety and effectiveness. Generally, Class III devices are those that are life sustaining or life supporting, implanted in the body, or present an unreasonable risk of illness or injury. New Class III devices must have approved premarket approval (PMA) applications. New Class III devices are those that were not marketed by anyone before May 28, 1976 (that is, postamendment). This is the date when the Amendments to the FD&C Act which specifically included medical devices went into effect.

Until PMAs are called for by regulation (at least 30 months must have elapsed since the final classification date before FDA can call for

a PMA for these products), someone marketing either a device that was commercially distributed before May 28, 1976 (preamendment), or a device substantially equivalent to the preamendment device, is subject only to general controls.

Panels of experts were established several years ago to provide advice and recommendations to FDA on device classification. After receiving the panel recommendations, FDA determines which class is appropriate and classifies the device by publishing in the *Federal Register* the classification for that device. A proposed classification regulation is then published in the *Federal Register* for public comment. After the comments are received and evaluated, a final classification regulation can be published. Proposed classification regulations have been published for all medical devices; however, not all of these have resulted in a final classification.

Class III is the most restrictive class and contains the fewest devices that aid the handicapped. Examples of Class III preamendment devices are stair-climbing wheelchairs and cochlear implants.

Q. How may a manufacturer obtain current information on the classification status of a device?

A. A manufacturer may contact the Center for Devices and Radiological Health to request this information. Informal inquiries about the present classification of any particular device should be directed to DSMA (800-638-2041). A written request should be sent to the Document Mail Center (HFZ-401), CDRH, FDA, 8757 Georgia Avenue, Silver Spring, Maryland, 20910.

Q. Before a final order on classification, what controls are applied to devices?

A. The general controls provisions of the Amendments apply to all devices currently being marketed. Following final classification, these controls continue to apply.

Devices for which a premarket notification [510(k)] was submitted, and found not "substantially equivalent" to medical devices on the market prior to May 28, 1976, must have an approved PMA. Manufacturers of these devices must also comply

with the investigational device exemption (IDE) regulation when they are doing clinical testing to substantiate safety and effectiveness.

IMPLANTABLE DEVICES

Devices intended to be implanted into the human body are usually in Class III, if they were marketed before May 28, 1976, even if they are found to be substantially equivalent to a device marketed before that date. Some implantable devices, however, are or will be in Class II. FDA may determine that premarket approval is not necessary for reasonable assurance of safety and effectiveness for any of these devices and place them into a different classification. An implantable device not marketed before May 28, 1976, and not substantially equivalent to a preamendment device may be marketed only if it has an approved PMA.

Total hip and knee prostheses are examples of implanted devices that are designed to aid handicapped/disabled individuals. Other devices such as limb prostheses may fall into the category of custom devices. (Custom devices are defined later in this brochure.)

Q. What is FDA's definition of an implanted device?

A. Although FDA has not established a formal definition of the device term "implant," working definitions have been published in the Classification Procedures and investigational device exemption regulations. These regulations define the term "implant" as a device that is:

- Inserted into a surgically or naturally formed cavity of the human body.

- Intended to remain there for a period of 30 days or more. FDA may, at its discretion, determine that devices placed in subjects for shorter periods are also implants.

Q. Could an implantable device for which a 510(k) is submitted be determined by CDRH to be substantially equivalent to a preamendment device even if it has significantly unique functional characteristics?

A. Yes, provided those functional changes do not significantly affect the device's safety and effectiveness.

Q. Who is responsible for the performance of a device once it has been implanted?

A. Before *and* after implantations, the manufacturer is responsible for assuring that a device is safe and effective. The health professional is responsible for using a device properly. Ultimate responsibility for a device failure depends on the specific facts of a given situation and requires case-by-case analysis.

Q. Can manufacturers of Class III implantable devices that are substantially equivalent to preamendment devices collaborate on the clinical data required for a PMA?

A. Yes. Manufacturers may collaborate when they submit PMAs providing clinical data to substantiate the safety and effectiveness of their respective devices.

DEVICES PREVIOUSLY REGULATED AS DRUGS (TRANSITIONAL DEVICES)

Certain articles previously regulated as drugs are now being regulated as devices. These "transitional" devices are automatically classified into Class III. Those devices that required a New Drug Application (NDA) require a PMA prior to marketing. Others that did not require an NDA are classified as either Class I or Class II devices. Thus, articles subject to approved NDAs are regarded as Class III devices with approved PMAs; pending NDAs likewise become pending PMAs.

The *Federal Register* of December 16, 1977, contains two lists of devices previously regulated as drugs: those devices for which premarket approval is needed, and those for which premarket approval is not needed. Since that time other products have been regulated as "transitional" devices, but no further lists have been published. The list includes devices for the handicapped such as soft contact and intraocular lens (in Class III) and dialysis fluids used in renal dialysis (Class II).

GENERAL CONTROLS

REGISTRATION AND LISTING

Manufacturers, repackagers, relabelers, and specification developers (firms that develop a product and then have someone else manufacture it) are required to register their establishments and list their devices with FDA. Initial distributors (importers) of foreign-made devices, must also register with FDA; however, they are required to list devices only in certain circumstances, i.e., if they also repackage the product. Form FDA 2891 is used for registration, while form FDA 2892 is used to list devices.

Manufacturers of raw materials or components used in manufacturing a finished device are exempted from registration if they do not market the same material or components directly to end users (i.e., as replacement parts) and are not engaged in selling these products only to device manufacturers. Examples of other establishments exempt from registration are:

- Licensed practitioners, including physicians, dentists, and optometrists, who manufacture or alter devices soley for use in their practice
- Pharmacies and other retail outlets who dispense or sell devices in the normal course of business
- Persons who manufacture devices solely for use in research, teaching, or analysis and who do not distribute such devices in commerce
- Warehousers and wholesalers who do not revise devices or their containers
- Carriers who receive, carry, hold, or deliver devices in their normal conduct of business
- Persons who dispense devices to the user or who render a service necessary to provide the user with a device or its benefits, i.e., those who dispense hearing aids, opticians, clinical laboratories, etc.

Foreign manufacturers are required to list those devices that they plan to sell in the United States. These firms are not required to

register with FDA; however, FDA encourages them to do so. Initial distributors of foreign manufactured devices comply with device listing regulations by identifying to FDA those foreign firms whose devices they import into this country.

Forms for establishment registration and device listing may be obtained from the Device Registration and Listing Branch (HFZ-342), CDRH, FDA, 8757 Georgia Avenue, Silver Spring, Maryland 20910 (301-427-7190).

Q. If a device is assembled from many parts, would the final assembler be regarded as the "manufacturer"?

A. Yes, although it is conceivable that accessories to devices (such as optional trays or IV supports for a wheelchair) may be included in the device as assembled or sold separately directly to the user. In this case, the assembler and the accessory manufacturer each would be regarded as a manufacturer.

Q. Is registration done only once?

A. No. Each establishment must be re-registered each year using FDA form 2891(a). FDA sends out this form in three separate mailings throughout the year beginning in May and ending in November. The manufacturer must complete Part Two of this form, including any necessary changes, and mail it to FDA within six weeks after receipt. Part One of the form is retained as proof of re-registration.

Q. What information is required on form FDA 2891?

A. Required information includes name, street address, city, state, and zip code of the device establishment; all other business trade names used by the establishment; name and address of the owner/operator of each establishment; name and address of the official correspondent; and estimated number of different devices manufactured.

Q. What changes in registration information have to be updated?

A. Any changes in individual ownership, corporate or partnership structure, official correspondent, or location of the registered loca-

tion are to be submitted by letter to the Device Registration and Listing Branch. The letter should include the current registration number and a statement indicating that the information reflects a change in a previous submission. This information must be submitted to FDA within 30 days of such changes. Any other changes may be made at the time of re-registration.

Q. Does the registration number assigned by FDA constitute FDA approval of the establishment or device?

A. No. Registration of an establishment or listing of a device does not in any way denote FDA approval of the establishment or its products.

Q. Are establishments exempted from registration subject to FDA inspection?

A. Yes. For example, as part of the inspection of the ultimate manufacturer of a device, the plant of a component manufacturer may be inspected.

PREMARKET NOTIFICATION

Device manufacturers who must register their establishments are also required to notify FDA at least 90 days before they intend to commercially distribute a device for the first time. This is known as a premarket notification or a 510(k). Firms are also required to notify FDA if they plan to reintroduce a device that has been significantly changed or modified to the extent that it could affect the safety or effectiveness of the device. Such a change or modification could relate to the design of the product; the type of material used; the product's chemical composition, energy source, or manufacturing process; or a new intended use. FDA uses the information in a 510(k) to determine whether the subject device is substantially equivalent to a device already classified by FDA. This mechanism can identify "new" devices (not in commercial distribution prior to May 28, 1976) that have not been classified. These "new" devices are automatically placed into Class III.

Each 510(k) should be submitted in duplicate and contain the following information:

- All names of the device, including trade (proprietary) name, i.e., Jones tele-aid; common (usual) name, i.e., handicapped phone; and the [classification] name assigned by the classification panel and found in the *Federal Register* announcement for that panel, i.e., powered communication system.

- Registration number (if applicable). A firm need not be registered to submit a 510(k). Registration is not required until 30 days after a firm has begun commercial distribution.

- Class of the device and the appropriate classification panel. If the device is not classified, a statement to that effect should be included in the 510(k).

- Actions taken to comply with performance standards for a Class II device that has a final FDA standard.

- Samples of proposed labels, labeling, and advertisements that describe the device, its intended uses, and directions for use.

- Statement of how the device is either similar to and/or different from other devices on the market, plus sufficient data to support the statement. These data may be in the form of specifications for the subject device vs. the specifications for similar devices or studies that support the labeled claims for the device.

- Information describing a significant change or modification, if any occurred, that could affect the device's safety or effectiveness.

Class II contains the greatest number of medical devices; this holds true for devices for the handicapped or disabled and will probably be true for orphan devices regardless of technology advances. The reason for this is that even with new technology, most devices have still been found substantially equivalent.

Q. How long does FDA have to review a 510(k)?

A. Ninety days - but see the questions and answers following for qualifications.

Q. If FDA receives an incomplete 510(k) and requests additional information to support it, does the 90-day period begin again?

A. Yes. If FDA requests additional information after the 510(k) was received, the 90-day period begins again. However, in many instances the full 90-day period will not be needed to complete the review.

Q. If a manufacturer who has submitted a 510(k) does not receive an answer from FDA within 90 days, what action should the manufacturer take?

A. CDRH usually answers the manufacturer within 90 days. If a manufacturer receives no answer within 90 days after the submission was received by FDA, the manufacturer may proceed to market the device. It is prudent, however, to determine FDA's response to the 510(k) by having DSMA (800-638-2041) determine whether or not the submission was received and the disposition of the submission.

Q. What is the definition of "commercial distribution"?

A. A device is in commercial distribution if it meets all the following conditions:

- The device was displayed, advertised, or otherwise offered for sale before May 28, 1976, for a specific intended purpose or purposes, with no limitations (e.g., no limitation to research or investigational use).

- The manufacturer had, before May 28, 1976, accepted or had been prepared to accept, at least one order to purchase the device that resulted, or would have resulted, in a sale of the device in the United States, generally with delivery to occur immediately or at some future date.

- The device was not being offered or accepted only for research or investigational use.

- The manufacturer of the device can provide adequate documentation establishing the three items above to the satisfaction of FDA.

Q. Does the submission of an IDE application, establishment registration form FDA 2891, or device listing form FDA 2892 fulfill the requirements for premarket notification?

A. No.

Q. Who does <u>not</u> need to submit a 510(k)?

A. Essentially, a 510(k) is not required for preamendment devices, devices under the investigational device exemption (IDE) regulation, transitional devices, and custom devices.

An exemption from the 510(k) requirements also applies to an "own-label" distributor and a repackager who places his own name on a device and does not change any other labeling or otherwise affect the device, provided that either:

- The device was in commercial distribution before the May 28, 1976, effective date of the Medical Device Amendments.
- A premarket notification was filed by another person.

A 510(k) submission is not required to resume commercial distribution of a device that was on the market before May 28, 1976, and discontinued by the manufacturer. Also, if a manufacturer has a PMA application pending before FDA, a 510(k) is not needed.

GOOD MANUFACTURING PRACTICES

The good manufacturing practices (GMP) regulation covers the methods, facilities, and controls used in manufacturing, packing, storing, and installing medical devices. It identifies the essential objectives that must be included in a quality assurance (QA) system. A QA program meeting the GMP requirements can ensure that finished devices meet specifications by reducing manufacturing process variation. Because the regulation covers a broad spectrum of devices, firms are allowed discretion in determining the necessity of certain steps and in developing procedures appropriate for the product. All medical device manufacturers, including manufacturers

of devices for the handicapped, must adhere to the GMP unless the device is exempted in a final classification regulation.

The GMP regulation designates two device categories: "critical" and "noncritical." Critical devices are defined as those intended to be surgically implanted into the human body or to support or sustain human life and whose failure, when used according to labeling instructions, could reasonably be expected to result in significant injury. General requirements apply to all devices, but critical devices must also meet additional GMP requirements. A list of "critical" devices was published in the *Federal Register* as part of the preamble to the GMP regulation. Only products that appear in this list are considered critical devices. As the list is updated, new products will be added and others may be deleted. If you have questions concerning the current status of your product, call the Division of Compliance Programs (301-427-7122) or DSMA (800-638-2041).

Q. Must a manufacturer of components of medical devices comply with the GMP regulation?

A. The manufacturer of "components" of medical devices is, in some cases, subject to GMPs. For example, when a manufacturer fabricates components exclusively for use in a finished medical device that is manufactured in the same facility as the components, the manufacturer has full control of the components manufacturing process. In such cases, component manufacturing is considered part of the production of the finished device and is subject to the applicable requirements of the GMP regulations. Manufacturers of components who supply only a fraction of their production to finished device manufacturers do not have to comply with the GMP regulations. For example, standard transistors, capacitors, etc. are not manufactured exclusively for use in devices. Part 820.1 of the GMP, however, encourages component manufacturers to use the GMP regulations as guidelines where appropriate.

Q. If a facility repairs a device, is it subject to the device GMP regulation?

A. Not if the facility simply repairs the device, returning it to its original condition, for a user. If a firm is in the business of marketing reconditioned devices, it must register and must comply with applicable GMP requirements. Modification that causes the

device to vary from original specifications is "manufacturing," and is subject to the GMP regulation.

PERFORMANCE STANDARDS

FDA has the authority to issue mandatory standards for Class II medical devices. To date none have been issued under this authority; however, CDRH has published its intention to begin preparation of mandatory standards for the following 11 medical devices:

- Continuous ventilator
- Vascular graft prosthesis of 6mm and greater diameter
- Cardiac monitors (including cardiotachometers and rate alarms)
- Ventilator tubing
- Breathing frequency monitors
- Central nervous system fluid shunts and components
- Toxoplasma gondii serological reagents
- Rheumatoid factor immunological test systems
- Calibrators for hemoglobin or hematocrit measurement
- Antimicrobial susceptibility test discs
- Immunoglobulins A, G, M, D, and E immunological test systems

Although none of the above devices would fall into the categories of devices specifically for the handicapped/disabled or orphan-type devices, they <u>are</u> in Class II and standards will eventually be written for these devices. Firms should be aware of the standards-setting process so they may provide input when the time comes.

Currently performance standards are in place for products regulated by CDRH under the Radiation Control for Health and Safety Act. The following medical device types fit into this category:

- Diagnostic x-ray systems
- Laser products
- Therapeutic ultrasound equipment
- Sunlamp products

Although standards have not been developed, special reporting procedures are required for:

- Diagnostic ultrasound and other medical ultrasound products
- Microwave diathermy and other medical microwave products

Q. How is a mandatory standard developed?

A. The law requires a five-step process to be announced in the *Federal Register* as follows:

- A notice announces the opportunity for interested persons to request that the device be reclassified from Class II to Class I or Class III.
- If the device is not reclassified, a notice invites interested persons or organizations to submit an existing standard or to offer to develop a standard.
- Upon receiving any offer, FDA may accept an existing standard, accept an offer to develop a standard, or proceed on its own to develop a standard.
- An announcement explains the proposed standard and requests comments. Any technical or scientific issues may be referred to an independent standards advisory committee.
- Upon resolution of any technical or scientific issues, FDA publishes the standard as a final regulation to become effective in one year.

Q. Must clinical trials ever be conducted in support of the safety and effectiveness of a Class II device? If so, must an investigational device exemption be obtained?

A. Clinical trials may be needed to establish that a given Class II device is as "safe and effective" as the marketed device to which "substantial equivalence" is claimed. Also, clinical trials may be required to establish a new use for an "old" device. However, the IDE regulation exempts a marketed device from clinical investigation when the investigation involves one of the labeled indications for use.

PREMARKET APPROVAL

Manufacturers of medical devices are required to obtain an approved premarket approval application (PMA) before they can market a Class III device. An approved PMA is, in effect, a private license granted to the applicant to market a particular medical device. Other firms seeking to market the same type product must also obtain an approved PMA. Premarket approval requirements are different for preamendment devices, postamendment devices, and "transitional" devices (devices regulated as new drugs or antibiotic drugs before May 28, 1976).

A preamendment device is one in commercial distribution (defined on page 11) before May 28, 1976, the enactment date of the Medical Device Amendments to the FD&C Act. Manufacturers of Class III preamendment devices are not automatically required to have an approved PMA in order to continue marketing. FDA must wait until at least 30 months have elapsed from the effective date of a final classification regulation or until 90 days after publication of a final regulation requiring the submission of a PMA, whichever period comes last, before requiring an approved PMA to continue marketing a preamendment medical device.

Postamendment devices are those commercially distributed after May 28, 1976. These may require either, neither, or both a 510(k) or PMA. A postamendment device fitting the description in a final classification regulation of a Class I device exempted from the 510(k) requirement is also exempted. By definition, all Class I and II devices are exempted from PMA requirements. Conversely, if the device fits the description of a Class I device that is not exempted, it too is not exempted. Postamendment Class II devices cannot be exempted from the 510(k) requirements. Devices for which a premarket notification has been submitted and a finding has been made of substantial equiv-

alence to a preamendment Class III device are subject to the same requirements as outlined above for the preamendment Class III counterpart. FDA determines substantial equivalence after reviewing the manufacturer's submission under section 510(k) of the FD&C Act.

Class III "transitional" devices and "new" devices (postamendment devices that are not substantially equivalent to preamendment devices or Class I or Class II postamendment devices) are Class III by statute and require a PMA or must be reclassified into Class I or Class II before being marketed. Manufacturers of these devices may either submit a PMA or petition FDA to reclassify the devices into Class I or Class II. Clinical studies in support of a PMA or a reclassification petition are subject to the IDE regulation. (See page 19, "Investigational Device Exemptions.")

When FDA receives a PMA, it makes a "threshhold" determination of whether the PMA is suitable for filing, that is, if it is sufficiently complete to permit a substantive review. An incomplete PMA is not filed until it is resubmitted with the needed information and is accepted for filing. The filing date is the date FDA receives what it accepts as the complete PMA; the 180-day review period provided by the FD&C Act is counted from this date. Significant changes may "stop" this 180-day "clock," which is "restarted" at zero when a new (amended) PMA is filed. For resubmitted PMAs, if accepted for filing, the 180-day period begins as of the day they were received by FDA. Once accepted for filing, the PMA undergoes scientific review by appropriate FDA personnel and advisory committees. FDA promptly notifies PMA applicants of any apparent deficiencies. After receiving recommendations from the advisory committee, FDA approves or denies approval of a PMA within the 180-day review period unless a longer period has been agreed upon by FDA and the applicant. FDA notifies the applicant of its decision by letter. A *Federal Register* notice is then published announcing the decision and the availability of a summary of the safety and effectiveness data on which the decision is based. This notice also provides the applicant and other interested persons an opportunity for administrative review of the FDA approval or denial action.

Medical devices that use the latest in technological advances are most likely to be considered "new" devices requiring PMAs. Prosthetic devices used to aid handicapped or disabled individuals and equipped with microprocessors are probably at the forefront of the

technological revolution and stand a good chance of requiring extensive testing to meet the PMA requirements.

Additional information on requirements for a PMA are available from the premarket approval staff (HFZ-402), Office of Device Evaluation, CDRH, FDA, 8757 Georgia Avenue, Silver Spring, Maryland 20910 (301-427-7445), or DSMA (800-638-2041).

Q Have any regulations requiring a PMA submission for preamendment devices been published in the Federal Register?

A. FDA proposed a rule requiring the filing of a PMA for the implanted cerebellar stimulator in the *Federal Register* of September 6, 1983. It also published a list of preamendment devices that have high priority for requirement of PMA filing. As of March, 1987, these include:

These include:

- Automated differential cell counters (notice of intent to reclassify)
- Automated heparin analyzers
- Automated blood cell separators
- Implantable pacemaker pulse generators
- Pacemaker programmers
- Replacement heart valves (proposal)
- Infant radiant warmers (notice of intent to reclassify being reviewed)
- Implanted diaphragmatic/phrenic nerve stimulators
- Implanted intracerebral/subcortical stimulators for pain relief (proposal)
- Transabdominal amnioscopes (fetoscopes) and accessories (final)

- Contraceptive intrauterine device and introducer (final)

- Contraceptive tubal occlusion devices and introducers (proposal)

Q. Must evidence of both safety and effectiveness be included in a PMA for Class III preamendment devices and for devices determined by FDA to be their substantial equivalent?

A. Each PMA must contain evidence of both safety and effectiveness. Sometimes, safety and effectiveness data on the device may be available in the literature. In such instances, the literature may be cited rather than submitted in the PMA itself. Requirements for data will be determined on an ad hoc basis.

Q. Can a product that has received approval under a PMA be advertised as "FDA approved"?

A. No. Reference to premarket approval, investigational device exemption, or any report or analysis resulting from an FDA inspection are prohibited. In addition, reference to establishment registration or a registration number may be misleading and result in a device being considered misbranded.

Manufacturers should avoid any representation that creates an impression of official approval of a device because of compliance with the FD&C Act or an FDA regulation.

INVESTIGATIONAL DEVICE EXEMPTIONS

To allow manufacturers of devices intended solely for investigational use to ship and use these devices on human subjects, the FD&C Act authorizes FDA to exempt these firms from certain of its requirements. This investigational device exemption (IDE) applies only to investigational studies involving human subjects that are undertaken to gather safety and effectiveness data for a medical device. Applicants for an IDE for a device considered to present "significant risk" must submit to FDA information demonstrating that testing will be supervised by an Institutional Review Board (IRB), that appropriate informed consent will be provided, and that

certain records and reports will be maintained. Submission of such information to FDA is not required for a "nonsignificant" risk device; however, IRB approval is still required.

The term significant risk is defined as an investigational device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject.

- Is purported or represented to be for use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject.

- Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject.

- Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

Certain types of devices are exempted from the IDE regulation. Other than the exemption for one-of-a-kind custom devices (what constitutes a custom device is explained in detail on page 23), and devices substantially equivalent to preamendment devices used for the same intended purpose as the preamendment device, products for the handicapped or disabled will not fit the exemptions.

FDA, under a bioresearch monitoring program, conducts inspections of sponsors, clinical investigators (testing involving human subjects), IRBs, and nonclinical laboratories (testing not involving human subjects) to assure validity of scientific data and compliance with the IDE requirements.

Q. Who decides whether a given device poses a "significant risk" as that term is used in the IDE regulation?

A. The local IRB decides whether or not a device proposed for clinical testing under its review will expose patients to a "significant risk." If the study comes to the attention of the FDA for some reason, FDA can overrule the IRB decision.

Q. Are devices in commercial distribution before May 28, 1976, exempt from IDE requirements?

A. In general, yes. The IDE regulation exempts preamendment devices, other then "transitional" devices, if they are used or investigated in accordance with labeling in effect before May 28, 1976. For Class II devices, this exemption expires on the effective date of a regulatory performance standard. If the devices do not meet the performance standard, they may be distributed only under an approved IDE. For Class III preamendment devices, this exemption expires 90 days after the effective date of the FDA regulation or order calling for a PMA submission.

Q. Are all devices marketed after May 28, 1976, subject to the IDE regulation?

A. Except for "transitional" devices, the IDE regulation exempts postamendment devices that FDA has determined to be substantially equivalent to preamendment devices if they are tested for claims made in the labeling that FDA reviewed when determining substantial equivalence.

Q. Is a device that introduces energy into a subject's body a significant risk device?

A. Such a device may be a significant risk device. However, the risk rating depends on the condition of the patient, conditions of use, device purpose, and power output.

Q. Is it possible for a device implanted for less than 30 days to be a significant risk device?

A. Yes. FDA may declare such a device to be a significant risk device, but the determination would be made on a case-by-case basis. The decision whether a product involves significant risk depends on the intended use of the device rather than on its nature as an implant.

Q. If a device has several uses, one of which involves significant risk, are investigations of the nonsignificant risk uses subject to the significant risk requirements of the IDE regulation?

A. No. They are subject only to those sections of the IDE regulation applicable to nonsignificant risk devices. If that same device is used in an investigation that presents significant risk, it is subject to the full IDE requirements for that use.

Q. What kind of testing is exempt from the IDE regulation?

A. The following testing is exempt:

- Consumer preference testing of devices, testing of a modification, or testing of a combination of two or more devices already in commercial distribution if the purpose of the testing testing is not to determine safety and effectiveness and does not put subjects at risk.
- Research testing for purposes other than determining the safety and effectiveness of a device for human use.
- Testing of devices:
  - That are legally in commercial distribution if the testing accords with the indications in the device's labeling.
  - That are intended solely for veterinary use.
  - That are shipped solely for research with laboratory animals and are labeled appropriately.
- Testing of diagnostic devices that comply with diagnostic device labeling requirements and that meet the following exemption criteria:
  - The testing is noninvasive.
  - Testing does not require an invasive sampling procedure that presents significant risk.
  - The device does not by design or intention introduce energy into a subject.
  - The device is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

In addition, the IDE regulation does not apply to fabrication of a custom device if the device is not being tested to determine safety and effectiveness for purposes of commercial distribution or to an intraocular lens subject to an approved IDE under the intraocular lens IDE regulations.

CUSTOM DEVICES

The term "custom device" is defined in the investigational device exemption (IDE) regulation as a device that:

- Necessarily deviates from devices generally available or from an applicable performance standard or premarket approval requirement in order to comply with the order of an individual physician or dentist.
- Is not generally available to, or generally used by, other physicians or dentist.
- Is not generally available in finished form for purchase or for dispensing by prescription.
- Is not offered for commercial distribution through labeling or advertising.
- Is intended for use by an individual patient named in the order of a physician or dentist, and is to be made in a specific form for that patient, or is intended to meet the special needs of the physician or dentist in the course of professional practice.

In less complex terminology, the term "custom device" refers to a device, ordered by physicians or dentists for use in their own practice or for a particular patient, that is not generally available in finished form and is not labeled or advertised for commercial distribution. Devices generally available to licensed practitioners cannot be considered custom devices.

Except for premarket notification, manufacturers of custom devices must comply with all the general control requirements for medical devices (GMPs, registration, listing, investigational use of devices, banning, restriction, adulteration, and misbranding). Cus-

tom devices are exempt from applicable performance standards, premarket approval and premarket notification requirements.

Traditionally, FDA has interpreted the term "custom device" very strictly; for this reason most devices claimed "custom" by their manufacturers are determined not to be custom devices by FDA.

Usually, examples of custom devices have been in the area of handicapped or disabled products. The most common reference is made to prosthetic devices customized to meet individual patient needs; e.g., artificial legs.

Q. What is meant by the term "generally available" mentioned above?

A. A custom device may not be an off-the-shelf item. It should not, for instance, appear in any catalog. It must be specifically tailored to meet the needs of one health professional in his practice or the needs of his patient. If there is any question whether or not a device is a custom device, advice should be obtained from the Division of Compliance Operations (HFZ-320), CDRH, FDA, 8757 Georgia Avenue, Silver Spring, Maryland 20910 (301-427-7218) or DSMA at (800-638-2041).

Q. Are custom devices exempt from the IDE regulation?

A. Yes, if the devices are not being tested to determine safety or effectiveness for purposes of commercial distribution. Custom devices are subject to all provisions of the FD&C Act except sections 510(k), Premarket Notification; 514, Performance Standards; and 515, Premarket Approval.

TRADE SECRETS AND CONFIDENTIAL INFORMATION

Certain sections of the FD&C Act concern confidentiality of information. The intent is to protect trade secrets and prohibit their use to a competitor's advantage. These provisions also give the public access to information necessary to assess the propriety of FDA actions with respect to devices.

A manufacturer may indicate that certain information submitted to FDA is regarded as trade secret; FDA, however, makes the final determination of what is a trade secret. This determination is based on the concept of competitive advantage, i.e., if knowledge about device characteristics gives the possessor the opportunity for an advantage over competitors.

FDA is prohibited from using trade secret information as the basis for reclassifying a device from Class III to Class II or for establishing or amending a performance standard for a reclassified device. To allow public scrutiny, FDA is required to prepare and distribute a detailed summary of safety and effectiveness information, including any adverse health effects, that was the basis for major decisions concerning a device.

It is a criminal act for anyone to use to their advantage or to disclose (other than to the courts) trade secret information. The critical issue, however, is the determination of what constitutes a trade secret. For Class I or Class II devices, except for material previously made public, safety and effectiveness data submitted to a classification panel is considered confidential until a decision on final classification is made.

FDA may release trade secret information essential for completion of a contract, to the contractor. This release of trade secrets and confidential information must be contingent upon the contractor's implementation of prescribed security precautions.

Q. What is a trade secret?

A. A trade secret may consist of any formula, pattern, device, or compilation of information used in one's business which gives the manufacturer an opportunity to obtain an advantage over competitors who do not know or use it.

Q. What is "confidential commercial or financial information"?

A. Confidential commercial or financial information is valuable data or information used in one's business that the manufacturer customarily holds in strict confidence or regards as privileged and does not disclose to any member of the public.

COLOR ADDITIVES FOR DEVICES

Devices containing color additives are adulterated unless there is a regulation listing the color for the intended use. A "listing" regulation identifies a color and it's specific use, either in general or in narrow terms. Provisions for color additives are limited to those that directly contact the body for a significant period of time. CDRH plans to issue guidance on color listing obligations of device manufacturers in the near future.

Q. How should a manufacturer proceed with respect to the use of color additives in or on devices?

A. Until proposed or final regulations are published by FDA, manufacturers may obtain approval to use or investigate a color additive in or on a device through a color additive petition. If a device is subject to premarket approval and contains a color additive, approval will not be given until the color is listed. A color listing enforcement policy has not been adopted for 510(k) reviews because these end with a substantially equivalent judgment, not FDA approval.

Manufacturers who wish to add a color additive to a device should submit a 510(k). They may want to consult with FDA to determine which approach to use and what type of data they will have to submit. For more information, contact the Division of Product Surveillance, HFZ-340, CDRH, FDA, 8757 Georgia Avenue, Silver Spring, Maryland 20910 (301-427-8156), or call the Division of Small Manufacturers Assistance (DSMA) at (800) 638-2041.

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Regulatory Requirements for Devices for the Handicapped

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